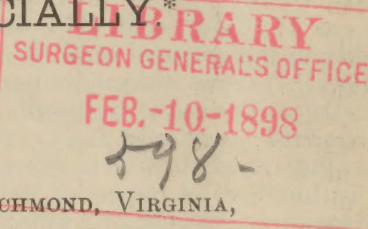


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REPORT ON THE
PROGRESS OF SERUM-THERAPY IN GENERAL:
IN VIRGINIA ESPECIALLY*

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Committee of Investigation appointed by the Richmond Academy of Medicine and Surgery, etc.

To the Fellows of the Richmond Academy of Medicine and Surgery:

Your committee, appointed April 13, 1897, begs leave to submit the following report upon "The Progress of Serum-therapy."

The first mention of the employment of the idea of serum therapy is that in the recorded practice of inoculating patients as a prophylactic measure against smallpox, employed at the beginning of the eighteenth century in Turkey. Inoculation gave way before the more desirable method of vaccination. The number of lives which Jenner's discovery has saved is well nigh incalculable. The first mention of the use of serum is to be found among the Germans, who employed the treatment under the name of *Isopathy*, about the middle of this century. To what extent it was used, and with what success it was credited by them, is not definitely stated, but it must have impressed them favorably, for a variety of isopathic preparations made their appearance under such names as "phthisin, hydrophobin, scarlatinin," etc.†

DIPHTHERIA.

The history of the development of the antitoxin treatment of diphtheria is so well known,

*Presented to the Richmond Academy of Medicine and Surgery, January 25, 1898, and, on motion, it was made the *Subject for Discussion* during the meeting held February 8.

† New York Medical Times, vol. 24, p. 67.

and its acceptance now so universal, that it would be useless, even if the limits of this report rendered it possible to go fully into details on these points. Even at the time that your committee was appointed it could be said that a sufficiently extensive trial of the antitoxin treatment of diphtheria had been made to remove the fears which many had entertained as to its action, and to place the remedy in an assured position as one of inestimable worth.

During the past year statistics from many and varied sources have appeared, all tending still further to increase the confidence of the profession in the remedy, and to demonstrate the saving of life which it has accomplished. Many who were sceptical have been convinced by the unanswerable argument of statistics whose authenticity could not be questioned, until to-day it may be said that but few physicians, indeed, who have given the subject careful consideration do not accord to the remedy even more value than was at first claimed for it by its staunchest advocates.

Only two sets of these statistics will be referred to, not because they are more favorable than others, but on account of the large number of cases recorded in them, and because they represent such diversity in the class of cases treated.

The report of the committee of the American Pediatric Society, presented at its last meeting, includes 1,704 cases of laryngeal diphthe-

presented by Committee.

ria which occurred in the practice of 422 physicians in the United States and Canada. In this report the following points are among the most prominent: Before the use of antitoxin it was estimated that 90 per cent. of laryngeal diphtheria cases required operation, whereas now, with the use of antitoxin, only 39.21 per cent. require it. The mortality in the whole series of 1,704 cases was 21.12 per cent. (360 deaths). In the non-operated cases the mortality was 17.18 per cent. (178 deaths). The mortality in the operated cases (27.24 per cent.—182 deaths) shows even more remarkable results. Before the use of antitoxin only 27 per cent. *recovered*; now only 27.24 per cent. *die*.

The other report to which reference will be made is the "Second Report of Medical Superintendents upon the Use of Antitoxic Serum in the Treatment of Diphtheria in the Hospitals of the Metropolitan Asylum's Board during the year 1896." (London). In these hospitals during 1896 antitoxin was used in 71.3 per cent. of all cases of diphtheria, the remedy not being employed in moribund, mild, or doubtful cases. The total death rate during 1896 (under antitoxin) was 20.8 per cent.; that of 1894 (without antitoxin), although then considered remarkably low, was 29.6 per cent. This represented a saving of 365 lives. It is well known, however, that only during the early days of the disease does antitoxin exert its full beneficial effect; and hence, while the above figures show a difference in the total death rate of only 8.8 per cent., the difference in cases treated on the first day was 17.8 per cent.; on the second day, 14.2 per cent.; on the third day, 11.7 per cent.; on the fourth day, 9.1 per cent., and on the fifth day or later, 6.2 per cent. Laryngeal cases were attended with a mortality of 62 per cent. in 1894; 29.6 per cent. in 1896. Operated laryngeal cases had a death rate of 70.4 per cent. in 1894; 41 per cent. in 1896. It is the opinion of the superintendents that there has been no reduction in the frequency of complications of the disease as a result of antitoxin treatment, except in the case of nephritis, which occurs less often. In fact, it would seem as if the other complications occur even more frequently than formerly. This, however, is only apparent, and is due to the closer observations which are now made, and, even more, to the fact that many severe cases, which would have died under other treatment, now recover, and these are naturally more prone to develop complications.

In this report the general results of antitoxin treatment are summed up as follows: 1. Diminution of faucial swelling; 2. Lessening of

irritating and offensive discharge from the nose; 3. Limitation of extension of membrane; 4. Earlier separation of exudate; 5. Limitation and earlier separation of membrane in laryngeal cases; 6. Improvement in general condition and aspect of patients; 7. Prolongation of life, in fatal cases, to an extent not obtained with former methods of treatment.

It has been claimed by those who refuse to recognize the value of diphtheria antitoxin, that the favorable results shown in the statistics of the past few years are due to other factors than the employment of antitoxin. By some it is held that the type of the disease has become milder; others that since the widespread application of bacteriologic diagnosis, cases are now called diphtheria which were formerly not so classified; or, again, that moribund cases and cases treated after the fifth day of the disease are excluded in many of the statistics. The first report to which reference has been made above, answers fully the first objection, since it deals with only laryngeal cases, and laryngeal diphtheria can never be considered mild. In the report of the Metropolitan Asylum's Board Hospitals mild as well as moribund cases were not injected. As regards the influence of bacteriologic diagnosis, it is a fact which no one acquainted with the subject will dispute that the number of cases which would formerly have been considered diphtheria, but which are now excluded from the statistics by bacteriologic investigation, far exceed those in which the reverse is true.

While the above are strong replies to the criticisms of the opponents of antitoxin, we are indebted to Park* for a table of statistics against which none of the usual objections can be urged. This table, compiled from the official records of Berlin, Paris and New York, shows the absolute death rate per 100,000 inhabitants in these cities from diphtheria and croup from 1886 to 1897 inclusive. There is here no room for asserting that the statistics have been twisted to favor any plan of treatment, that any special class of cases has been excluded or included, and yet the reduction in mortality in all three of these cities since the introduction of antitoxin is remarkable and too uniform to be the result of mere coincidence. This table is of such interest that it is here appended:

* Park, Wm. H.: Contributions of Bacteriology to Therapeutics. Wesley M. Carpenter Lecture for 1897.

ABSOLUTE DEATH RATE FROM DIPHTHERIA AND CROUP PER 100,000 POPULATION.

Year.	Berlin.	Paris.	New York.
1886.....	125.7	73.2	187.5
1887.....	100.7	76.9	206.6
1888.....	76.1	83.7	167.7
1889.....	85.6	79.9	146.2
1890.....	102.0	77.5	110.6
1891.....	67.5	63.0	118.7
1892.....	92.9	63.6	123.3
1893.....	100.8	51.4	145.5
1894.....	86.7	40.7	158.5
1895.....	†59.7	17.7	105.2
1896.....	30.9	17.6	91.3
*1897.....	26.4	17.2	86.4

*Last quarter of year estimated.

†General use of antitoxin commended.

As regards actual advances in the antitoxin treatment of diphtheria, the chief of these seems to be the production of more potent and trustworthy serums and the attention to details in its manufacture, whereby its efficacy has been increased and many of its objectionable features diminished. Rashes and joint symptoms following its use are now somewhat less frequent than formerly.

The preparation of dried serum has not yet been brought to a sufficient degree of perfection to supplant the ordinary product, while "we have no more hope than we had five years ago of separating antitoxin completely from the horse serum."*

During the past few months the Health Department of New York city has been testing the comparative frequency of rashes after the use of filtered and unfiltered serums. Your committee is indebted to Dr. Wm. L. Somerset, Resident Physician Willard Parker Hospital, for the following statement, which is an approximate one, of the results obtained: Previous to the employment of filtered serum, rashes occurred at the Willard Parker Hospital in from 25 to 30 per cent. of all cases; since the use of filtered and unfiltered serum in parallel cases, the percentage of rashes where filtered serum was injected has been reduced to about 15 per cent., while it has risen to about 40 per cent. where the unfiltered product was employed. The higher percentage of rashes in the latter class of cases than formerly, is due to the fact that the unfiltered serum used in these cases contained the residue from the filtered portion. It would thus appear that the production of rashes is caused largely by some constituent of the serum which is incapable of passing, or passes only in small amounts, through unglazed porcelain.

* Park, loc. cit.

The use of antitoxin as a prophylactic measure has been steadily gaining ground, and with the production of a serum from which all objectionable features have been eliminated, its use in this direction will doubtless become even more popular; though, from the temporary nature of the immunity afforded, it must remain a measure to be adopted only in the presence of epidemics or in cases where exposure has undoubtedly occurred.

YELLOW FEVER.

In 1854 and 1855, inoculation, as a preventive measure, was made use of in Havana during an epidemic of yellow fever. In 1887, this idea was again introduced and followed up very thoroughly in Brazil. But in neither instance were the results satisfactory. In 1892, Domingo Freire introduced a diluted virus derived from the micrococcus xanthogenicus, which he held to be the etiological factor in the development of yellow fever. This diluted virus was advocated as a preventive inoculation by Dr. Belinger, of San Francisco, Dr. J. McFadden Gaston, of Atlanta, and others during 1893 and 1894; but the results have been disappointing. About the same time, in 1893, Dr A. S. Ashmead recommended "Murray's immunizing method" as follows: Inoculate with the blood serum of a partially immune subject (negro), and inoculate a second time with perfectly immune blood serum of a white subject who has had yellow fever. Before inoculation, however, as frost always modifies the virus, let the infected serum be first exposed to frost. Follow at once with a second inoculation of immune blood serum." Disappointments likewise followed the use of this method.

In July, 1897, Prof. G. Sanarelli, of the University of Montevideo, isolated and cultivated a bacillus which he considers to be the specific organism of yellow fever. Probably it is the same bacillus as that formerly described by Surgeon General Sternberg. Possibly both may ultimately be proven to be secondary invaders. However, Sanarelli has been occupying himself since last summer in the securing of a protective or curative serum, about which most encouraging reports have been already made. And yet scarcely is the hope born that at length we have a protective or curative agent with which to meet yellow fever before adverse reports are coming in to indicate that we must wait and see.

TUBERCULOSIS.

The medical world was startled in 1890 by

the announcement that Koch had discovered a remedial agent for phthisis. This announcement was hailed with joy, and it was immediately put to the clinical test, but its virtues, so ably set forth by its discoverer, soon began to minimize, and finally it fell into disrepute as a curative remedy. Since the introduction of tuberculin, several serums have been brought forward, and have been tried with varying success by many physicians.

Among the most popular of these preparations are the serum of Prof. E. Maragliano, of Genoa, obtained from the dog, the ass, and the horse. When treatment was begun as late as the formation of cavities in the lungs, he claims a *cure* of 7.76 per cent. In non-febrile tuberculosis, his successes have amounted to nearly 100 per cent. of recoveries. He recommends that 1 c. c. of the serum should be the dose injected subcutaneously every second day. In febrile forms, the dose may be increased for several days—5 to 8 days—to 5 and even 10 c. c. Such are the contradictory reports as regards successful use of Maragliano's serum by different doctors that it is difficult to come to a fixed opinion on the subject.

What has been said in general of Maragliano serum applies in the main to the published results of the use of the antitubercle serum introduced in 1895 by Dr. Paul Paquin, of St. Louis. That it is useful when administered with other remedies is more than probable.

Early in 1896, Koch introduced what he called T. R. Tuberculin, and this was followed by encouraging reports of its use. But it was not long before the process of its manufacture was found to be faulty in that, notwithstanding the centrifugation, it was discovered that in a large number of the preparations on the market tubercle bacilli remained in the fluid. This being recognized as an error of manufacture, it has been withdrawn from market—certainly until the fault of its manufacture can be remedied.

Antiphthisin is a sozalbumin, introduced some years ago by Klebs, which he regards as the germicidal part of tuberculin. Von Ruck "attests its absolute safety, and considers that it has curative properties."

But the early disappointments in practice of the serum treatment of tuberculosis have made the profession skeptical as to the remunerative value of any and all such methods of treatment; and yet it is evident to the non-skeptical who reviews the experience of unbiased practitioners that it is probable that whatever may be found curative of tuberculosis, one of the measures to be used will be perfection of

some of the antitoxines so-called. It is the opinion of many that the scientific worker is getting in the neighborhood of the real remedy, and is probably knocking at a door of the house in which the truth is to be found.

TYPHOID FEVER.

Chantemesse and Widal found, in 1888, that susceptible animals could be rendered immune by inoculating them with a culture of the typhoid organisms which had been rendered sterile by heat.

Following this line of investigation, serum-therapy has been employed in typhoid fever. However, with the most persistent use of this substance, the results in this disease have been unsatisfactory.

SCARLET FEVER.

An antistreptococcic serum has been employed in this affection, and while it does not seem to have any efficacy in the scarlet fever itself, yet, from a certain number of observations made by Roux, it appears to have a favorable influence on the complications due to the streptococcus, and which are so common in this malady.

TYPHUS FEVER.

In a prison at Bongie, from November 25th to December 12th, 40 cases occurred, with two deaths. Serum-therapy was commenced December 12th, the serum being obtained from patients who had recovered. From 2 to 6 c.c. were injected into each of 39 cases, and only one died. Legrain noted fall of temperature, improvement in pulse, disappearance of fever, and the severe cases soon became mild in type.

Although this disease is rare, owing to improved hygienic measures, yet, from the favorable report of serum in its treatment, it is to be hoped that the rate of mortality will be kept lowered in those instances where the disease gains a foothold.

RABIES.

Tizzoni and Cattani reported that serum of animals, rendered immune to hydrophobia, has the power of conferring immunity and arresting the disease when already developed. So far no trial has been made in man. If successful here, its value will surpass the treatment of Pasteur, in that the latter may produce immunity, but cannot cure the disease if once developed.

LEPROSY.

Carrasquilla treated a number of cases of leprosy with serum, and in fifteen cases of the

TABLE No. 1.—SHOWING A TABULATED STATEMENT OF THE REPORTED FACTS IN ONE HUNDRED CASES OF DIPHTHERIA OCCURRING IN THE PRIVATE PRACTICE OF VIRGINIA PHYSICIANS.

Number.	Sex.	Age.	Location of membrane.	Severity.	Was bacteriologic examination made?	Was it positive or negative?	Day of injection.	Whose preparation was used?	Dose.		Time of improvement.	Effect on temperature.	Effect on pulse.	Effect on general condition.	Was injection repeated?	How soon after initial dose?	Dose.		Effect on temperature.	Effect on pulse.	Effect on general condition.	Operation.	Disappearance of membrane (day).	Complications (usual).	Effect of serum on same.	Outcome of case.	Were there any rashes?	Character of rashes.	Joint affections.
									Units.	C. C.							Units.	C. C.											
1	F.	30 yrs.	t. and p.	Severe.	No.	Not stated.	2	P., D. & Co.	750	?	6 hours.	Fell 3°.	Reduced.	Not stated.	No.										R	No.		No.	
2	"	6 "	t. p. n. buccal, vaginal.	"	Yes.	Positive.	7 to 8	Behring's.	800	8	24 "	Increased at first; then fell.	Increased; then slowed.	Improved.	Yes.	3 days.	800		Increased.	Increased.	Bad.		Acute Nephritis.	?	R	Yes.	Gen. macular.	Yes.	
3	"	3 "	t. p. and l.	Malignant.	No.	Not stated.	1	"	?	2½	12 "	Reduced.	Reduced.	"	"	12 hours.	2½		Reduced to normal.	Reduced.	Improved.		No.		R	No.		No.	
4	"	11 mos.	t. p. n. and l.	Severe.	"	"	2	P., D. & Co.	1000	?	None in 24 hours.	No effect.	Not perceptible.	No effect in 24 hours.	"	24 "	1500	?	Reduced.	"	"		"		R	"		"	
5	M.	4 yrs. 2 mos.	l.	"	Yes.	Positive.	4	"	2000		16 hours.	Decreased.	Decreased.	Improved.	No.						Not stated.		Albuminuria	?	R	"		"	
6	F.	5 yrs.	t. and n.	"	No.	Not stated.	3	"	1000	5	16 "	"	"	"	"									R	Not stated.			Not stated.	
7	M.	3 "	l.	Malignant.	"	"	5	Behring.	1000	?	12 "	"	Improvement	?	"						Not stated.		"		R	"		"	
8	F.	5 "	t. and p.	Mild.	"	"	2	P., D. & Co.	1000	?	2 hours.	Increased.	Increased.	Improved.	Yes.	8 hours.	1500	?	Increased.	Increased.	Improved.		Not stated.		R	"		"	
9	"	3 "	l.	Severe.	"	"	4	"	1500		24 "	Reduced.	Reduced.	"	No.						Not stated.		"		R	"		"	
10	"	4 "	t. and p.	Mild.	"	"	4	"	1000		24 "	Reduced.	Reduced.	"	"								"		R	"		"	
11	M.	7 "	t. and p.	"	"	"	3	Pasteur Inst.	?	10	18 "	Not stated.	Not stated.	Not stated.	Not stated.								"		R	Yes.	Gen. urticaria	No.	
12	F.	14 "	t.	Severe.	"	"	6	Behring.	1500	6	12 "	Improved.	Improved.	Improved.	No.								"		R	No.		"	
13	M.	4 "	l. and t.	Malignant.	Yes.	Positive.	3	"	2000	8	Few "	Not stated.	Not stated.	"	Yes.	6 hours.	1000	4	Not stated.	Not stated.	Not stated.	No.	Not stated.		R	Not stated.		"	
14	"	22 mos.	l. and t.	Severe.	"	"	3	"	2100	8.4	18 "	"	"	"	"	18 "	1000	?	"	"	"	"	"		R	"		Not stated.	
15	F.	5 yrs.	l. and t.	"	"	"	5	Mulford & Behring.	1500	6	12-14 "	"	"	"	No.								"		R	"		"	
16	"	4 yrs. 6 mos.	l. and t.	"	"	"	4	Behring.	1800	7.2	8-10 "	"	"	"	Yes.	18 hours.	1000	4	Not stated.	Not stated.	Not stated.	"	"		R	"		"	
17	M.	5 yrs.	t.	Mild.	"	"	2	Mulford's.	1000	4	24 "	Reduced to normal.	Reduced to normal.	"	No.								"		R	"		"	
18	"	3 "	l.	Severe.	No.	Not stated.	3	P., D. & Co.	1000	?	6 "	Reduced.	Improved.	"	"						No.		"		R	"		"	
19	F.	30 "	p. and n.	"	"	"	3	"	1000	?	?	"	Reduced.	"	Yes.	24 hours.	1000	?	Reduced.	Increased.	Improved.				R	"		"	
20	"	2 yrs. 6 mos.	general.	Malignant.	"	"	4	"	?	?	4 hours.	"	"	"	"	8 "	?		"	Reduced.	"	Not stated.		"		R	Yes.	Urticaria.	"
21	"	5 "	l.	Severe.	Yes.	Negative.	3	"	500	?	2-3 "	Not stated.	Not stated.	"	"	24 "	1000	?	Not stated.	Not stated.	"	No.			R	?		"	
22	M.	4 mos.	t. l. p. and n.	Malignant.	No.	Not stated.	2	"	?	?	Not stated.	"	"	Not stated.	Not stated.	8 hours.	?		?	?	Improved.		Not stated.		R	Not stated.		No.	
23	"	12 yrs.	t. and p.	"	"	"	3	"	?	?	6 to 8 hours.	"	"	Improved.	Yes.	8 hours.	?		?	?	"		Paralysis.	?	R	"		Not stated.	
24	F.	16 "	l.	"	Yes.	Positive.	5	Behring's.	?	?	12 "	Reduced.	Reduced.	"	"	12 "	?		Reduced to normal.	Reduced to normal.	"	Not stated.			R	"		"	
25	M.	4 "	l.	"	No.	Not stated.	?	"	?	?	?	Not stated.	Not stated.	Not stated.	Not stated.								"		R	"		"	
26	"	7 "	p.	Severe.	"	"	4	Mulford's.	?	10	12 hours.	Reduced.	Reduced.	Improved.	No.								"		R	"		"	
27	"	10 yrs. 3 mos.	l. and p.	Malignant.	"	"	4	P., D. & Co.	?	?	10 "	"	"	"	"						Not stated.		Feeble heart action.		R	"		"	
28	Not stated	22 mos.	l. t. and p.	Severe.	"	"	2	"	500		12 "	"	"	"	Yes.	12 hours.	1500		Improved.	Improved.	Improved.	No.	Not stated.		R	"		"	
29	M.	8 yrs.	t. p. and n.	"	"	"	2	"	1500	6	12 "	"	"	"	No.								"		R	"		"	
30	"	7 "	l.	Malignant.	"	"	2	"	1000		Not stated.	Not stated.	Not stated.	Not stated.	Yes; thrice.	7, 12 and 12 hrs.	1000 each.		Reduced.	Reduced.	Improved.	No.	Not stated.		R	"		"	
31	F.	18 "	t.	Mild.	"	"	2	"	1500		12 hours.	Reduced.	Reduced.	Good.	No.								Albuminuria	Not stated.	R	Yes.	Urticaria.	"	
32	"	30 "	l.	Severe.	"	"	7	"	1500		30 "	None.	None.	Not stated.	Yes.	22 hours.	1500		Reduced.	Reduced.	Improved.	No.	Albuminuria and broncho-pneumonia.	Not stated.	D	"	?	"	
33	M.	18 mos.	t.	"	"	"	4	Behr., No. 2.	600		Not stated.	Not stated.	Not stated.	"	No.								"		R	Not stated.		"	
34	"	2 yrs. 6 mos.	t.	Mild.	"	"	3	"	750		"	"	"	"	"								"		R	"		"	
35	"	2 yrs.	t.	"	"	"	2	"	700		10 hours.	Reduced.	"	Improved.	"								"		R	"		"	
36	"	6 "	t.	Severe.	"	"	5	"	1000		Not stated.	Not stated.	Reduced.	"	"								"		R	"		"	
37	"	4 "	l.	Mild.	"	"	2	U. S. M. H. S.	4		24 hours.	Reduced.	Reduced.	"	Yes.	36 hours.	4		Improved.	Improved.	Improved.	No.	Not stated.		R	"		"	
38	F.	16 "	t. and p.	Severe.	Yes.	Positive.	3	"	10		8 "	"	"	"	Yes; twice.	12 and 36 hrs.	10 c. c. each.		Reduced.	Reduced.	"		Albuminuria	Unaffected.	R	"		"	
39	M.	26 "	t. and p.	"	"	"	2	"	10		Not stated.	"	"	"	No.	24 hours.	5		Reduced.	Reduced.	Improved.		No.		R	Yes.	Urticaria.	"	
40	F.	5 "	t.	Mild.	"	"	12	"	5		10 "	"	"	"	No.	24 hours.	5		Reduced.	Reduced.	Improved.		"		R	No.		"	
41	"	3 yrs. 6 mos.	t.	"	"	"	3	Behring's.	4		8 hours.	"	Improved.	Not improved	Yes.	24 hours.	5		Not affected.	Not affected.	Not stated.	Tracheotomy.	Diph-croup.	Influenced.	D	"		No.	
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anæsthetic type secured a remarkable degree of success. Medina, commenting on this treatment, sums up as follows:*

"The sensation is restored more or less rapidly according to the extent and gravity of the lesions of the peripheral nervous system. Distinct patches lose their abnormal color without disappearing entirely. Œdema subsided rapidly in some cases, slowly in others. The skin shrinks and resumes its physiological condition after the absorption of the œdema. The tubercular variety shrinks, breaks down, and disappears by absorption, desquamation, or suppuration, leaving traces of their existence at the affected spots. Ulcers, after having presented copious purulent secretions, rapidly clear off and are covered with healthy skin; scars from former suppurative lepromata fade and tend to assume the same level as the surrounding skin. Ulcerated mucous membranes fade like the skin and recover sensibility, while the tubercles break down. The face loses its leonine appearance. Lastly, the patient recovers his appetite, the ability to sleep, and the mental state improves."

SARCOMA AND CARCINOMA.

Varying success has attended the use of bacterial products in inoperable malignant disease. Coley, who has done a great deal of work in this class of cases, secured greater success with the treatment in sarcoma than in carcinoma. The conclusions of the New York Surgical Society, which may be considered as a conservative survey of the efficacy of this treatment in malignant diseases, are as follows:†

"(1) The danger to the patient from the treatment is great.

(2) The alleged successes are so few and doubtful, the most that can be said for the treatment is that it may offer a slight chance of improvement.

(3) valuable time has been lost in operable cases by giving the treatment a trial before operating.

(4) The method should be absolutely confined to inoperable cases."

SYPHILIS.

Richet and Haricourt were the first to try injections of serum in the treatment of syphilis. They report two cases, one resulting in a cure, the other showed marked signs of improvement—the ulcerated surface decreasing four-fifths in size. Pellizzari and Neuman have

employed blood in its treatment, but no satisfactory results were obtained.

STREPTOCOCCIC INFECTIONS.

In *erysipelas*, Marmoreck used the antistreptococcic serum in 413 cases in which the mortality was 3.87 per cent. against 5 per cent. prior to the use of serum. In 165 cases of *erysipelas* alone, the mortality was 1.2 per cent. As a result of the use of the serum, he noticed an improvement in the general condition, fall of temperature, and local improvement.

Puerperal fever has been treated by this plan with a certain degree of success. It has not proven as useful in this disease as there was reason to expect at the first mentioning of the subject.

The serum has also been used with success in acute hæmorrhagic septicæmia, *erysipelas neonatorum*, acute general septic peritonitis, purulent cellulitis of the face, cerebro spinal meningitis, etc.

PNEUMONIA.

Klemperer, in 1892 and 1893, published his researches as to the treatment of serum therapy in six cases with good results. Mosny, Bonone, Emmerich, and Pansini following up this idea, obtained practically the same results as Klemperer. On the other hand, Hughes and Carter, in 1894, reported the injection of the serum of patients just recovered from pneumonia in ten cases of this disease, and they had no reason to consider the treatment efficacious.

CHOLERA.

Many experiments have been made in cholera, chiefly as inoculations, and these mostly in animals until recently. During an epidemic of this dread malady in Spain, 50 per cent. of those attacked died. After inoculation was used, the rate of mortality was reduced to 25 per cent.

INFLUENZA.

The bacteria of influenza was discovered in 1892. Rabbits were inoculated with cultures, and after they had been proven immune, the blood serum was used on men suffering from influenza with varying success.

TETANUS.

Behring and Kitasato were the first to produce in the blood of animals a distinctly potent and valuable antitoxic substance. In 1892, Dr. Rudolph Schwarz reported the first success with tetanus antitoxin in man. Cases of cure have been reported from time to time which

*Report to the National Academy of Medicine of Columbia, at Bogota, 1895.

†Annals of Surgery, July, 1896.

gradually increase the per cent. of recoveries. It may be very properly asked why the success with serum in this disease is not so favorable as that in diphtheria—the two antitoxins being “so nearly identical in their efficacy as agents for immunization?” The answer may be found “in the manner” in which “the two infections begin and progress.”* “The tetanus affection advances for from five to ten days undetected in the wound, the toxins develop unnoticed, cause their deleterious effect, and only after general poisoning has occurred is the disease detected.

The diphtheria infection starts on the surface, and before its toxins are fully developed and absorbed, it is diagnosticated by the appearance of its exudate, the husky voice, or the nasal obstruction. At this time we could also arrest the tetanus infection. If we allow this time to pass by, then, as in tetanus, after the constitutional poisoning has taken place, the antitoxin is usually of no avail.”

An improvement in the form of tetanus antitoxin is the solid variety. It is claimed that this preparation can be kept indefinitely, and is ready for use at any time by simply dissolving it in water.

The serum treatment has been extended considerably in its scope, so that at the present time few of the more infectious diseases, to which mankind is liable, have not been considered by the experimental bacteriologist. In addition to the diseases above referred to, may be mentioned the *bubonic plague*, anthrax, alcoholism, acute delirians mania, glanders, pleuropneumonia, foot and mouth disease, chicken cholera, hog cholera, and bites of reptiles, as other diseases in which serum-therapy has been employed.

SERUM THERAPY IN VIRGINIA.

Having briefly reviewed the progress of serum therapy from its incipency up to the present time, the committee thought it advisable to ascertain the extent to which this class of remedies had been employed in our own State. With this object in view, circular letters were sent to the members of the Medical Society of Virginia, and to such other physicians in the State as the committee had reason to believe had employed serum treatment. In this communication information was requested under four headings—diphtheria, tuberculosis, tetanus, and the diseases for which antistreptococcic serum is employed. Under the respective headings replies were sought upon the

leading points of interest likely to arise in the course of the disease under consideration.

In response to about one thousand of the above letters of inquiry, the committee received reports from seventy-nine physicians. Thirty-five of these state that they have not employed serum in their practice, giving as their reason, in all but four instances, lack of opportunity to test the same. The reason of non-employment of the remedy by these four is stated to be disbelief either in the efficacy of the treatment or in the theory upon which its application is founded.

Of the forty-four who have employed serum, thirty-one used it in diphtheria alone; six in tuberculosis; one in tetanus; four in diphtheria and tuberculosis; one in diphtheria and tetanus, and one in diphtheria and puerperal sepsis. The total number of cases reported was 151, there being 100 cases of diphtheria, 48 of tuberculosis, two of tetanus and one of puerperal sepsis.

The committee feels confident that these figures do not represent the entire number of cases in which antitoxin treatment has been employed in Virginia. Although every effort was made to secure reports from all physicians in the State who had employed serum treatment, many who have used the remedy failed to respond to the letters of inquiry, and in other instances the reports were received too late for tabulation.

The reports received on diphtheria embrace one hundred cases occurring in the practice of thirty-seven physicians. The following tables, compiled from these reports, show the results obtained:

TABLE II.—Classification of Cases.

Laryngeal.....	14
Laryngeal and tonsillar.....	4
Laryngeal and pharyngeal.....	2
Laryngeal, tonsillar and pharyngeal.....	3
Laryngeal and nasal.....	1
Tonsillar.....	12
Pharyngeal.....	7
Nasal.....	1
Tonsillar and pharyngeal.....	14
Tonsillar and nasal.....	1
Tonsillar, pharyngeal and nasal.....	3
Pharyngeal and nasal.....	1
Tonsillar, pharyngeal, nasal, buccal and vaginal.....	1
General.....	3
Not stated.....	33
Total.....	100

* The Wesley M. Carpenter Lecture for 1897. By Wm. H. Park, M. D.

TABLE III.—*Type of Disease.*

Type.	Cases.	Cured.	Died.	Per Cent. of Deaths.
Laryngeal.....	24	21	*3	12.50
Non-laryngeal	43	40	**3	6.97
Not stated.....	33	31	2	6.06
Total.....	100	92	8	8.00

* One death from broncho-pneumonia 21 days after disappearance of membrane.

** One case moribund when first injected.

TABLE IV.—*Severity of Disease.*

Type.	Cases.	Cured.	Died.	Per Cent. of Deaths.
Mild.....	14	13	*1	7.14
Severe.....	39	37	2	5.13
Malignant.....	20	17	3	15.00
Not stated.....	27	25	2	7.41
Total.....	100	92	8	8.00

* A case of tonsillar and pharyngeal diphtheria in a child of five years; 1,500 units injected on second day of illness; 1,500 units eight hours later. Died suddenly four hours after second injection.

TABLE V.—*Bacteriologic Examination.*

	Cases.	Cured.	Died.	Per Cent. Died.
Made; result positive	23	21	2	8.70
" " negative	*1	1	0	0.00
Not made.....	39	35	4	10.25
Not stated.....	37	35	2	5.40
Total.....	100	92	8	8.00

* Laryngeal.

TABLE VI.—*Day of Injection.*

Injected on	Cases.	Cured.	Died.	Per Cent. of Deaths.
First day of illness...	3	3	0	0.00
Second day of illness	15	13	*2	13.33
Third day of illness.	17	15	2	11.76
Fourth day of illness	9	9	0	0.00
Fifth day of illness..	5	5	0	0.00
After five days.....	7	5	2	28.57
Not stated.....	44	42	2	4.54
Total.....	100	92	8	8.00

* Case noted in Table IV.

TABLE VII.—*Serum Used.*

Name of Maker.	Cases.	Cured.	Died.	Per Cent. of Deaths.
Behring.....	26	24	2	7.69
Roux	1	1	0	0.00
Parke, Davis & Co...	29	27	2	6.90
H. K. Mulford Co....	4	4	0	0.00
U. S. Marine Hospital.....	6	5	1	16.67
Not stated.....	34	31	3	8.82
Total.....	100	92	8	8.00

TABLE VIII.—*Initial Dose.*

Number of Units	Cases.	Cured.	Died.	Per Cent. of Deaths.
Under 500.....	1	1	0	0.00
500-1,000.....	9	8	1	11.11
1,000-1,500.....	15	14	1	6.67
1,500-2,000.....	16	15	1	6.25
Over 2,000.....	2	2	0	0.00
Not stated.....	57	52	5	8.77
Total.....	100	92	8	8.00

TABLE IX.—*Repetition of Injection.*

Was Dose Repeated.	Cases.	Cured.	Died.	Per Cent. of Deaths.
Repeated..				
500-1000	3	2	1	33.33
1000-1500	9	9	0	0.00
No. units } 1500-2000	4	2	2	50.00
Over 2000	*1	1	0	0.00
Not stat'd	**37	33	4	10.50
Not Repeated....	25	25	0	0.00
Not stated.....	21	20	1	4.76
Total.....	100	92	8	8.00

* Repeated three times, 1,000 units at each injection.

** One case repeated twice.

Average time of improvement after injection of antitoxin, in 47 cases stated, 12.1 hours.

Average time of disappearance of membrane, in fifty cases stated, 7.1 days.

Rashes occurred as a result of the antitoxin in eight cases—seven urticarial and one macular. Joint affections occurred in two cases. The less frequent occurrence of these symptoms after the administration of antitoxin shows an improvement which may fairly be attributed to the smaller amount of serum which it is necessary to inject since higher potencies have come into general use; although the possibility of the occurrence of rashes being overlooked in private practice should not be forgotten.

Of the twenty-four laryngeal cases reported, three were operated (tracheotomy) with two recoveries and one death. Unfortunately, dosage was not stated in any operated cases.

Complications. Albuminuria occurred in seven cases, one of which seemed to be favorably influenced by the antitoxin. In one case with complications of broncho pneumonia, acute nephritis and paralysis, these complications improved after second injection.

Of the hundred cases reported, all except one were in white subjects.

The total number of cases reported is rather small to permit of deductions in certain directions, and this fact is also responsible for the appearance of certain discrepancies in the above tables. Thus the mortality in cases reported as mild (7.14 per cent.) is greater than that in cases reported as severe (5.13 per cent.). There was only one death among the mild cases, the cause of which was not clear to the physician, but this one death has the effect of causing in the table the curious result noted.

Of the fatal cases, one was moribund when injected. One died of broncho pneumonia, on the thirty-third day of illness, three weeks after complete disappearance of the membrane. The third fatal case, one of laryngeal diphtheria, was not seen "until a few hours before stenosis required operation" (tracheotomy). In this case, there was temporary improvement after the first injection. The fourth fatal case, one of laryngeal and nasal diphtheria in a colored infant ten months of age, was brought from a distance to the office of the physician who administered the serum. Two injections, 500 units each, of antitoxin were given, resulting in some improvement. The child died on the day following the second injection, under circumstances not known to the physician reporting the case. In three of the fatal cases, no data whatsoever were given. In the eighth fatal case, attributed to heart failure, the attending physician, in making his report, states, "I think the serum must have had something to do with the cardiac failure."

The above report, showing a mortality of only eight cases in a hundred, in one of the most dreaded and hitherto fatal of the acute infectious diseases, is in keeping with the universally favorable statistics which have, from time to time, been tabulated and published from other sources, both in hospital and private practice. Although, from the number of reports received, it will be seen that Virginia physicians have followed a conservative course in adopting this method of treatment, yet the popularity of the remedy is steadily and rapidly increasing.

While appreciating the valuable assistance rendered the committee in this, the first attempt in the State to collect data relating to any special line of treatment, it was to be expected that the resulting report could not be wholly satisfactory, owing to the incomplete nature of many of the individual reports received. The difficulty encountered by the committee from this source emphasizes the advisability of physicians keeping a careful and accurate record of important cases, especially those treated by methods whose full value is still under investigation.

A glance at the above tables will show that upon even the most important points the information was, in many instances, deficient.

Thus the age of patient was not stated in 34 cases; type of disease in 33 cases; severity of disease, in 27 cases; day of injection, in 44 cases, and dose of antitoxin, in 57 cases—yet, these are the five most important and vital factors in the compilation of statistics relating to diphtheria as treated by antitoxin.

In only 24 cases was a bacteriologic examination made. The importance of having bacteriologic confirmation of the clinical diagnosis is, apparently, not yet as generally appreciated as it should be by the profession at large. In those cases where the diagnosis of diphtheria is obvious from clinical evidence alone, antitoxin should be administered at once without waiting for a bacteriologic examination. In doubtful cases, where the physician, though not positive, is inclined to regard the case as diphtheria, the same course should be adopted, especially if the case seem urgent. In that class of still more doubtful cases, where the ablest clinician is unable to arrive at even an approximate diagnosis, bacteriologic investigation is imperative, and should not be neglected if it can possibly be secured.

In all the above instances, however, even where antitoxin has been administered at once, the clinical diagnosis should be confirmed bacteriologically wherever practicable.

From a critical review of the reports received the fact has impressed itself upon the committee that a certain degree of timidity still exists with many physicians in the employment of the remedy. The dose given in many instances is still too small, and the necessity of as early administration as possible seems to be not yet fully appreciated. With increased experience, and a more thorough understanding of the indications for its employment in the proper dosage, there is reason to hope that its usefulness will be still further extended.

TUBERCULOSIS.

Your committee regrets that the information

furnished upon the serum treatment of this disease in our State is so meagre and incomplete that accurate deductions on the subject cannot be made. Of the 48 cases reported, five were cured, 13 improved, 13 unimproved, 15 died, and two not stated.

Concerning the five cases reported as recovered, no information was given as to stage of disease when treatment was begun; the diagnosis of cure was made upon the improvement in physical signs and the disappearance of tubercle bacilli from the sputum; two of these cases are stated to be in robust health and free from all signs of tuberculous taint.

Of the 13 cases improved, one was in the first stage of the disease, and under the treatment all symptoms improved, but the bacilli, although diminished in number, still persisted. Concerning the other 12 cases, no data were given.

Of the 13 unimproved cases—in one, a case in the second stage of the disease, treatment had to be discontinued on account of unfavorable action of the serum. Concerning the other 12 unimproved cases, no data were given.

Of the 15 cases terminating in death, one was in the first stage when treatment was begun; three in the second stage; five in the third stage; and six not stated.

In the majority of cases in which information upon the subject was furnished, untoward symptoms followed the injections and were apparently due to the serum.

In six cases, rashes of an urticarial, macular, or erythematous character were noted; in three cases, there were joint symptoms, and in three, alarming attacks of general numbness, apnoea, syncope, or collapse, followed the injections.

From the information furnished in the reports received, it appears that serum-therapy does not, at the present time, offer any advantage over other methods of treatment in tuberculosis. Only one physician states that "serum-therapy is a great help to creosote, strychnia, etc., in the treatment of tuberculosis."

TETANUS.

Reports of only two cases of the employment of serum in tetanus were received—one mild, the other severe—both terminating fatally.

PUERPERAL SEPSIS.

The only instance reported of the employment of antistreptococcic serum was in a case of puerperal sepsis, following delivery by a colored midwife. The disease developed six days after delivery, and when treatment was begun, three days later, patient had a temperature of 103° Fahr., pulse 148. Improvement began sixteen hours after injection, and was

manifested by a fall in temperature of three degrees. In addition to the serum, the usual local treatment of curettage, douches, etc., was employed.

CONCLUSIONS.

Antitoxin is the most valuable remedy yet devised in the treatment of diphtheria.

Its use is especially valuable in laryngeal cases.

It should be employed at the earliest possible moment after a diagnosis is made.

The initial dose should be (according to the type and severity of the case) from 1,000 to 3,000 units of a concentrated serum, and should be repeated according to indications.

Local and other general treatment should not be neglected because antitoxin is used.

As a prophylactic agent, its value is unquestioned.

From the information furnished in the reports received, it appears that serum does not, at the present time, offer any advantage over other methods of treatment in tuberculosis.

The number of reported cases in tetanus and puerperal sepsis are too few to justify any conclusions.

The committee desire to extend to the following members of the profession their thanks for the report of cases and information:

Baird, J. W., Carsley, Va.
Barham, S. B., Spottsville, Va.
Bramblett, W. H., Pulaski, Va.
Corrie, Geo., Blossom Hill, Va.
Crawford, Joel, Yale, Va.
Ewell, Jesse, Ruckersville, Va.
Harker, F. S., Richmond, Va.
Harrison, Edmund, Richmond, Va.
Henley, Leonard, Williamsburg, Va.
Kerr, A. F., Millboro, Va.
Peek, Jesse H., Hampton, Va.
Scott, John W., Gordonsville, Va.
Simmons, John W., Floyd, Va.
Stoakley, Wm. S., Millboro Springs, Va.
Taylor, T. J., Walthall's Store, Va.
Wallace, J. W., Covington, Va.

Respectfully submitted.

The following physicians report that they have used serum-therapy:

Atkinson, B. M., Staunton, Va.
Blanton, C. A., Richmond, Va.
Brower, C. F., Catharpin, Va.
Dupuy, H. R., Norfolk, Va.
Edwards, Landon B., Richmond, Va.
Ellis, D. S., Ashland, Va.
Feild, E. E., Norfolk, Va.
Flannagan, L. E., Charlottesville, Va.
Frost, Henry, Marshall, Va.

Gibson, Wm. Alexandria, Va.
 Gleaves, C. W., Wytheville, Va.
 Hartman, W. F., Swoope, Va.
 Henkel, A. M., Staunton, Va.
 Henkel, H. H., Staunton, Va.
 Henson, J. W., Richmond, Va.
 Hoge, M. D. Jr., Richmond, Va.
 Hutchison, Frederick, Arcola, Va.
 Ingram, Lawrence, Manchester, Va.
 Jones, T. M., Alexandria, Va.
 Jordan, Arthur, Richmond, Va.
 Keen, T. F., Hamilton, Va.
 Kelly, J. W., Big Stone Gap, Va.
 Lankford, L., Norfolk, Va.
 Levy, E. C., Richmond, Va.
 Levy, H. H., Richmond, Va.
 Martin, Rawley W., Lynchburg, Va.
 McGuire, Hugh, Alexandria, Va.
 McGuire, Stuart, Richmond, Va.
 McMurran, R. L., Portsmouth, Va.
 Nelson, A. J., Gaines Mill, Va.
 Nelson, Hugh T., Charlottesville, Va.
 Nickolls, R. Angus, Richmond, Va.
 O'Brien, M. W., Alexandria, Va.
 Parkins, T. M., Mt. Sidney, Va.
 Patterson, J. K., Lynchburg, Va.
 Ross, George, Richmond, Va.
 Shepherd, L. C., Norfolk, Va.
 Slaughter, R. M., Theological Seminary, Va.
 Taylor, Hugh M., Richmond, Va.
 Tompkins, Chris., Richmond, Va.
 Tompkins, J. E., Fredericksburg, Va.
 Turner, W. D., Fergusson's Wharf, Va.
 Vanderslice, G. K., Phœbus, Va.
 ??? (FIVE failed to sign their names).

The following physicians report that they have not used serum-therapy:

Cannaday, A. A., Roanoke, Va.
 Copeland, J. E., Round Hill, Va.
 Doyle, C. W., Glendoyle, Va.
 Gillespie, R. B., Tazewell, Va.
 Gordon, H. W., Madison, Va.
 Holladay, Lewis H., Orange, Va.
 Holloway, R. G., Rappahannock Acad., Va.
 Massey, C. R., Post Oak, Va.
 Melvin, H. B., Houston, Va.
 Morton, C. S., Pamplin City, Va.
 Nuckolls, C. B., Hillsville, Va.
 Powell, E. C., San Marino, Va.
 Seward, R. Lee, Isle of Wight, Va.
 Wood, A. D., Martinsville, Va.
 ??? (one failed to sign his name.)

[POSTSCRIPT.—Since the tabulation of the *Report on Diphtheria*, an able practitioner sends in reports of two cases which may be added and percentages made on 102 cases of diphtheria instead of 100 as in the Tabulated Report].

	CASE I.	CLASS II.
Sex	Male.	Female.
Race	White.	White.
Age	Three years.	Four years.
Type.....	Laryngeal.	Tonsillar and nasal.
Clinical type.....	Malignant.	Malignant.
Bacteriological investigation.....	No.	No.
Serum injected.....	Third day.	First day.
Preparation used...	P. D. & Co.	P. D. & Co.
Initial dose.....	1000 units.	500 units (1 bulb).
Improvement manifest.....	In six hours.	None after first dose.
Temperature.....	Reduced.	No effect.
Pulse.....	Less frequent.	" "
Respiration.....	Less frequent and less laborious.	" "
General condition..	Improved.	" "
Injection repeated.	No.	Yes.
Indication for repetition.....	...	Lack of improvement.
Interval after initial dose.....	...	14 hours.
Dosage.....	...	1000 units repeated in 24 and 48 hours.
Effect on temperature.....	...	Reduced.
Effect on pulse.....	...	None.
Effect on respiration.....	...	Slower.
Effect on general condition.....	...	Gradual return to normal.
Other treatment employed.....	Calomel 1-12 grain. Pulv. ipecac $\frac{1}{2}$ gr. M. S. Repeat one every hour—six doses.	1-30 gr. mercury bichlorid. with 1-40 gr. strychnine.
Intubation or tracheotomy.....	No.	No.
Membrane entirely disappeared.....	On 6th day.	On 5th day.
Complications of disease.....	None.	Yes. Paralysis of voice complete. Very much shortened by serum.
Final outcome of case.....	Recovery.	Recovery.
Used antitoxin as prophylactic?.....	No.	No.
Rashes noted after antitoxin.....	None.	None.
Joint symptoms after antitoxin.....	None.	None.
		[This child was taken with diphtheria just as improvement from meningitis [cerebral or cerebro-spinal?] took place.—Editor.]